Typhoid fever in children – Emergence of resistant strains of typhoid fever in Pakistan

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Emerging resistance of typhoid fever in Pakistan is one of the key issue and main danger faced by the pediatric population. It is sparing neither any region nor any of the pediatric age. The situation has become a major threat for this age group in the last few years[1]. Enteric fever is classified in three types. The three types are non-resistant typhoid fever, multidrug resistant (MDR) or extensive drug resistant (XDR) typhoid fever. The three types of enteric fever are non-resistant, multi-drug resistant and extensively drug resistant. The presence of extensively drug resistant (XDR) typhoid fever caused by antimicrobial resistant (AMR) strains is increasing day by day[2].

The problem was first identified in Pakistan in the Hyderabad district of Sindh in November 2016 RDSRU over a period of almost 2 year (2016-2018) reported 8188 cases including more than 60% (5274) cases)of XDR typhoid. The maximum number of patients was from Karachi city making 60 % of the patients, followed by Hyderabad (27%). So a big chunk of patients was from these two major cities of Sindh. Pakistan is among one of the highly prevalent typhoid fever countries of the world [3]. The main reason for the spread of enteric fever is unavailability of clean drinking water and poor sanitation. The prevalence of enteric fever, MDR and XDR cases are increasing and at the same time health regularity authority supervise the rational use of antibiotics. The resistance strain to first line drugs like ceftriaxone is H58 is found has been found Pakistan[4].

The issue of XDR typhoid fever was taken as emergency and in the beginning of 2017 the government of Pakistan and took several important steps to control the serious issue wisely. These included public and students' awareness, availability of clean and medically fit water by providing chlorine tablets to the affected community.

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The clinicians were also sensitized on rational use of antibiotics. The children were also vaccinated initially two types of vaccines were in use until very recently. These two vaccines available included an oral enteric coated capsule type (Ty21a vaccine) used once daily for three days and an injectable form Vi polysaccharide vaccine (ViCPS vaccine) used as single dose intramuscular vaccine. Both the vaccines are not recommended in children below two years of age and one has to revaccinate after three years due to reduction in the efficacy. Therefore both the vaccines are not that much adoptable in pediatric age vaccination program [5,6].

Due to this alarming situation in Sindh, government of Pakistan started vaccination in August 2017, by vaccinating approximately 6,000 children, age 6 months to 10 years with Vi polysaccharide vaccine (*ViPS*). Later on campaigns were continued with typhoid conjugate vaccines (TCV) from January 2018. During these campaigns almost 118,000 children, age 6 months to 10 year were vaccinated. WHO did tremendous job in sustaining efforts regarding antimicrobial resistance (AMR) including initiatives like Global Antimicrobial Resistance Survival System (GLASS), supporting XDR National Task Force in Pakistan and Global Antibiotic and Development Partnership (GARDP) and encouraging public private partnership on research including enteric fever[7].

The government of Punjab also started mass pediatric age immunization with TCV in 2020. Pakistan Pediatric Association Punjab has taken a keen interest in making the program successful by conducting seminars in almost all major cities and districts of Punjab regarding the growing resistance pattern of the enteric fever. But the current situation of typhoid fever, MDR and XDR typhoid fever is an emergency and the situation can be overcome with ease by adopting very simple and affordable public measures like availability of safe drinking water, improving sanitation measures, taking hygiene measures by food handler, rationale use of antibiotics and making TCV as part of the immunization schedule[9]. The adoption of vaccination policy must be for all children but be started from the most deserving and outspread regions. The patients with suspicion of enteric fever must be examined by pediatricians of the regions and blood of the patient should be sent for culture

and sensitivity to know about the sensitivity pattern[8]. The efficacy of third generation was established in the management of enteric fever till few years back[9].No doubt the situation is very alarming and discouraging regarding the sensitivity pattern; as azithromycin is the only first line, oral and affordable drugs showing sensitivity to the typhoid fever in most of the regions of the country[10]. In complicated cases the Carbapenem group is effective[11]. This is time that we must have facility for knowing the resistance strain of the typhoid fever, adopt on all safe water and standard sanitation measures and vaccinate our population especially pediatric ones to curb this menace in time.

References:

1. Parry CM,Ribeiro,Walia K,Rupali P, Baker S, Basnyat B. Multidrug resistant enteric fever in South Asia: unmet medical needs and opportunities. BMJ 2019; 364:322.
2. Browne AJ , Hamadani BHK, Kumaran EAP Rao P , Longbottom J , Harriss E. Drug-resistant enteric fever worldwide, 1990 to 2018: a systematic review and meta-analysis. BMC Med 2020; 18:1-22.
3. Yousafzai MT, Irfan S, Thobani RS, Kazi AM, Hotwani A, Memon AM et al. Burden of culture confirmed enteric fever cases in Karachi, Pakistan: Surveillance for enteric fever in Asia Project (SEAP), 2016–2019. Clin Infect Dis 2020; 71(S3):S 214–21.
4. Yousafzai MT, Qamar FN, Shakoor S, Saleem K, Lohana H , Karim S. Ceftriaxone-resistant *Salmonella* Typhi Outbreak in Hyderabad City of Sindh, Pakistan: High Time for the Introduction of Typhoid Conjugate Vaccine. Clin Infect Dis 2019; 68: S16–S21.
5. Andrews JR, Qamar FN, Charles RC, Rya n ET. Extensively drug-resistant typhoid - are conjugate vaccines arriving just in time? N Engl J Med 2018; 379:1493-5.
6. Andrews JR, Baker S, Marks F. Typhoid conjugate vaccines: a new tool in the fight against antimicrobial resistance. Lancet Infect Dis 2018:S1473-3099(18)30350-5.
7. Farah NazQamar FN1, Batool R 1, Qureshi S , Ali M, Sadaf T, Mehmood J, Iqbal K et al. Strategies to improve coverage of Typhoid Conjugate Vaccine (TCV) immunization campaign in Karachi, Pakistan.Vaccines 2020; 8(697):1-12.
8. Naveed A, Ahmed Z. Treatment of Typhoid Fever in Children: Comparison of Efficacy of Ciprofloxacin with Ceftriaxone. Eur Sci J 2016; 12(6): 1857-7881.
9. Brockett S, Wolfe MK, Hamot A, Appiah GD, Eric D. Mint ED, Lantagne D. Associations among water, sanitation, and hygiene, and food exposures and typhoid fever in case–control studies: A systematic review and meta-analysis. Am J Trop Med Hyg 2020; 103(3): 1020–1031.
10. Qureshi S, Naveed AB, Yousafzai MT, Ahmad K, Ansari S, Lohana. Response of extensively drug resistant *Salmonella* Typhi to treatment with meropenem and azithromycin, in Pakistan. PLoSNegl Trop Dis 2020; 14(10): e0008682. https://doi.org/10.1371/journal.pntd.0008682
11. Hussain A, Satti L, Hanif F, Zehra NM, Nadeem S, Bangash TM Peter A. Typhoidal Salmonella strains in Pakistan: an impending threat of extensively drug-resistant Salmonella Typhi. Eur J Clin Microbiol Inf Dis. 2019; 38:2145–2149.